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| 09/915,780      | 07/26/2001  | Harn-Jing Terng      | 12674-003001        | 6948             |

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| EXAMINER    |
| TUNG, JOYCE |

|          |              |
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| ART UNIT | PAPER NUMBER |
| 1637     |              |

DATE MAILED: 05/21/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.  
**09/915,780**

Applicant(s)  
**Terng et al.**

Examiner  
**Joyce Tung**

Art Unit  
**1637**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on Mar 10, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above, claim(s) 10-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 23-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claims 1-36 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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### **DETAILED ACTION**

1<sup>1</sup> This application contains claims 10-22 drawn to an invention nonelected without traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

2. The amendment filed 3/10/2003 has been entered. Following the entry of the amendment, claims 1-36 are pending.

3. The objection of claims 3-5, 23, 26-28 and 30-31 under 37 CFR 1.75 as being a substantial duplicate of claims 7-9, 29, 32-37 is withdrawn.

4. The rejection of claims 27-28 and 33 under 35 U.S.C. 112, second paragraph is withdrawn.

5. The application complies with the Sequence Rules.

#### ***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 5-6, 9, 23-26, 28-29, 31-32, and 34-35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Drazen et al. (6,156,503) in view of Drmanac et al. (6,383,742).

Drazen et al. disclose a method and kit of identifying individuals at risk for an adverse response to  $\beta$ -agonist therapy (See column 1, lines 51-54). The method involves using allelic specific primer (See column 11, lines 12-26). The primer of Drazen et al. has a mismatch at penultimate position from the 3' end (under lined) which was changed from T to A (See column 11, lines 17-26) and a segment of nucleotide located immediately 5' to the second base is complementary to a part of target nucleic acid (the nucleic acid) (See column 11, lines 17-26).

Drazen et al. do not disclose that the primer comprises a binding member of a specific binding pair covalently bonded to the 5' end of the primer.

Drmanac et al. disclose a method of detecting a target nucleic acid species involving using labeled probe (See the Abstract). The label can be ligands which can serve as specific binding members to a labeled antibody, chemiluminescers, enzymes, antibodies which can serve as a specific binding pair member for a labeled ligand (See column 18, lines 64-67 to column 19,

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lines 1-4). Drmanac et al. also disclose the use of CovaLink NH strips for covalent binding of DNA molecules at the 5' end (See column 22, lines 1-14).

One of ordinary skill in the art would have been motivated to modify the primer of Drazen et al. by applying the teachings of Drmanac et al. (See column 18, lines 64-67 to column 19, lines 1-4 and column 22, lines 1-14 ) with a binding member of a specific binding pair covalently bonded to the 5' end of the segment. The motivation is that by using the binding member of a specific binding pair at 5' end of the nucleic acid probe, a small number of nucleic acid sample can be quickly identified (See column 6, lines 64-67). It would have been prima facie obvious to apply the binding member of a specific binding pair covalently bonded to the 5' end of the DNA molecule in the teachings of Drmanac et al. to the primer of Drazen et al. in order to identify the bindings of the discrimination primer.

Applicant's arguments filed 3/10/2003 have been fully considered but they are not persuasive. The response argues that neither Drazen nor Drmanac discloses that the first binding member is not labeled directly or indirectly. However, the newly added language "the first binding member is not labeled directly or indirectly" is unclear whether the first binding member is labeled directly or indirectly. Nevertheless, claim 1 at least requires that a first binding member of a specific binding pair is covalently bonded to the 5' terminus of the segment.

The teachings of Drazen et al. indicate that the primer is labeled and the detection can be done by oligonucleotide hybridization under appropriate conditions (See column 15, lines 6-27). Drmanac et al. disclose the use of CovaLink NH strips for covalent binding of DNA molecules at

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the 5' end (See column 22, lines 1-14). The teachings of Dramac et al. would satisfy the newly added limitations. The rejection is maintained.

8. Claims 3-4, 7-8, 26, 30, 32 and 36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Drazen et al. (6,156,503) in view of Drmanac et al. (6,383,742) as applied to claims 1-2, 5-6, 9, 23-26, 28-29, 31-32, and 34-35 above, and further in view of Higuchi et al. (5,994,056).

Drazen et al. disclose a method and kit of identifying individuals at risk for an adverse response to  $\beta$ -agonist therapy (See column 1, lines 51-54). The method involves using allelic specific primer (See column 11, lines 12-26). The primer of Drazen et al. has a mismatch at penultimate position from the 3' end (under lined) which was changed from T to A (See column 11, lines 17-26) and a segment of nucleotide located immediately 5' to the second base is complementary to a part of target nucleic acid (the nucleic acid) (See column 11, lines 17-26).

Drmanac et al. disclose a method of detecting a target nucleic acid species involving using labeled probe (See the Abstract). The label can be ligands which can serve as specific binding members to a labeled antibody, chemiluminescers, enzymes, antibodies which can serve as a specific binding pair member for a labeled ligand (See column 18, lines 64-67 to column 19, lines 1-4). Drmanac et al. also disclose the use of CovaLink NH strips for covalent binding of DNA molecules at the 5' end (See column 22, lines 1-14).

Drazen et al. and Drmanac et al. do not disclose that the binding member is an oligonucleotide 6-50 nucleotide in length and not complementary to any part of the nucleic acid.

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Higuchi et al. disclose an improved method for nucleic acid detection via polymerase chain reaction (See the Abstract). Higuchi et al. also disclose a primer which have non-complementary sequence added to the 5' end. The "tails" are useful for engineering particular restriction sites or other purposes. It is useful for increasing signal strength in the presence of genomic DNA (See column 14, lines 32-47). Higuchi et al. disclose that the choice of primers for use in PCR determines the specificity of the amplification reaction. The primer is sufficiently long to prime the extension products in the polymerization agent and typically contains 10-30 nucleotides, although that exact number is not critical to the successful application of the method (See column 8, lines 29-41). A non-complementary nucleotide fragment may be attached to the 5' end of the primer with the remainder of the primer sequence (See column 8, lines 51-58).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the primer of Drazen et al. with a non-complementary sequence to a target nucleic acid at 5' end because of the advantage of using the non-complementary sequence tail as taught by Higuchi et al. (See column 14, lines 32-47).

Additionally, one of ordinary skill in the art would have made the non-complementary sequence tail with 10-40 nucleotides in length because the probes which have the length of 10-40 nucleotides provide a specific hybridization binding to a target sequence. The motivation is that a primer containing 10-30 nucleotides is sufficiently long to determine the specificity of the amplification (See column 8, lines 29-41). It would have been prima facie obvious to modify the primer of Drazen et al. with a non-complementary sequence to a target nucleic acid at 5' end in

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the teachings of Higuchi et al. in order to make the discrimination primer. Therefore, the rejection is maintained.

The response argues that Higuchi et al. do not teach the first binding member that is not labeled directly. However, as indicated in section 11 below, the newly added language “the first binding member is not labeled directly or indirectly” is unclear how the primer is labeled. Nevertheless, claim 1 requires that a first binding member of a specific binding pair covalently bonded to the 5' terminus of the segment which is discussed in section 7 above. Higuchi et al. disclose a primer which have non-complementary sequence added to the 5' end. Thus, the rejection is maintained.

***NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT***

***Claim Rejections - 35 USC § 112***

9. Claim 1-9, and 23-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly added language “the first binding member is not labeled directly or indirectly” appears that the primer of the instant invention is not labeled. As disclosed in the specification the primer has a binding member at 5' end of the primer (see pg. 8, lines 3-10). Thus, it constitutes new matter.



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10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-9 and 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-9 and 23-36 are vague and indefinite because the newly added language “the first binding member is not labeled directly or indirectly” is unclear as to whether the primer is labeled or not.

#### ***SUMMARY***

12. No claims are allowable.

#### ***CONCLUSION***

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

May 6, 2003

  
GARY BENZION, Ph.D.  
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